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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,249	02/15/2002	Emanuela Mundo	10822-21	8612

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 01/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,249	MUNDO ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendments filed in the response on 5/23/05 under 37 CFR 1.312 have been entered.

Claims 8-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/18/2004.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's Declaration under Rule 1.132.

Maintained Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as set forth previously and reiterated below, because the specification, while being enabling for determining the susceptibility of Bipolar I or Bipolar II patients to antidepressant-induced mania related to Bipolar Disorder, wherein the antidepressant is the pro-serotonergic agent, does not reasonably provide enablement for determining the susceptibility of any patients to antidepressant-induced mania, wherein the patient is anyone treated with any antidepressant or where the antidepressant-

induced mania is related to another mood or anxiety disorder, such as unipolar depression or obsessive-compulsive disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, lack of sufficient guidance in the specification and the breadth of the claims.

The claims as written are broad and encompass any patient and any antidepressant – induced mania induced by any antidepressant. The specification does not enable the broad scope of the claims, which encompasses all patient populations treated with any antidepressant and antidepressant-induced mania related to any disorders.

The specification teaches (page 6, lines 19-20) that the patient is any patient being treated with antidepressants, preferably a patient with Bipolar Disorder who is being treated with an antidepressant that acts directly or indirectly on the 5HTT sites. The specification discloses (page 1, lines 11-13) that induction of mania in patients treated with antidepressants is complex and has been described to occur in Bipolar (BP), Unipolar (UP), and Obsessive-Compulsive (OCD) disorders; however (page 1, lines 17-19), "more recently it has become clearer that the phenomenon of antidepressant-induced mania is strictly related to a diagnosis of BP." The specification also teaches (page 1, line 24-26) an antidepressant-induced manic episode occurs in patients with BP independent from the treatment status (antidepressant or electroconvulsive therapy), and (page 1, line 28-29) the rate of induction of mania is higher in BP patients treated

with TCAs and MAOIs than in BP patients treated with SSRIs demonstrating that various antidepressants may produce differing incidences or occurrences of antidepressant-induced mania.

Furthermore, the art discloses that antidepressant-induced mania remains controversial; particularly antidepressant-induced mania lacks a consensus definition within the field as to what constitutes a switch into mania and how to reasonably attribute the switch to antidepressant use, may be associated with all antidepressants but with varying levels that may be patient-specific (Goldberg *et. al.*, 2003, *Bipolar Disorders*, 5:407-420), remains controversial in unipolar depression and may be the natural course of illness in bipolar patients (Chun *et. al.*, 2004, *Bipolar Disorders* 6:32-42).

The specification does not teach that the method can be practiced with antidepressant-induced mania related to other disorders, but discloses, "Antidepressant-induced mania is strictly related to a diagnosis of BP (page 1, line 18-19)". The specification does not teach the method can be practiced in patients with unipolar depression, obsessive-compulsive disorder, or all disorders treated with antidepressants. Finally, the specification does not teach that the method can be practiced with all possible antidepressants, which have different mechanisms of action, including selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine and sertraline that increase serotonin levels; tricyclic antidepressants (TCAs), such as amitriptyline, imipramine, and nortriptyline; monoamine oxidase inhibitors (MAOIs), such as anylcypromine and phenelzine, which block or inhibit, the action of the enzyme monoamine oxidase; and heterocyclics, such as bupropion and trazodone. Due to the large quantity of experimentation necessary to determine if other patients, including those specifically treated with antidepressants

for disorders other than BP develop antidepressant-induced mania and antidepressants other than pro-serotonergic agents can be used, the lack of direction/guidance presented in the specification regarding whether the type of antidepressant treatment including dose effect the risk of developing an antidepressant-induced mania and whether antidepressant-induced mania occurs with other disorders, the absence of working examples directed to same, the complex nature of the invention in which antidepressant-induced mania remains controversial as a bona fide form of mania or a side effect of drug therapy or a predisposed phenomenon, and the state of the prior art which established the unpredictability of antidepressant-induced mania related to other antidepressant disorders and the varying association with various antidepressants, and the breadth of the claims which fail to recite functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The specification provides essentially no guidance as to which of the essentially infinite possible patients is likely to be susceptible and the skilled artisan would not expect all patients or all patients using antidepressants to be susceptible to antidepressant-induced mania. Thus, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims.

Citing several papers in the literature Applicant argues that antidepressant-induced mania is a phenomenon that can be observed in any patient on antidepressants, e.g. those with bipolar, major depressive disorder or obsessive-compulsive disorder; and that this phenomenon can be observed in many classes of antidepressants and no just limited to the serotonergic agents. This argument has been fully considered but not deemed persuasive. Applicant's statements are not in dispute, but nor do such assertions contradict the basis of the rejection. Rather, the

specification has demonstrated a correlation between a particular antidepressant –induced mania and a particular allele, i.e. that between a particular class of antidepressant (SSRI) in a particular patient population and a particular serotonin transporter promoter allele. The claims, however, attempt to extrapolate this isolated correlation to all antidepressant-induced manias and this particular allele; yet neither the specification nor the prior art support such an extrapolation. As set forth above, and even Mundo et al., Letter to the Editor of Hospital and Community Psychiatry, 44(7)689, 1993, supplied by Applicant, discuss the poorly understood relationships between obsessive-compulsive disorder and mania, e.g. they state that the biological and clinical correlates of serotonergic function deficit seem to be contradictory (see the 3rd parapraph of col 4 of page 689. "Tossing out the mere germ of an idea does not constitute enabling disclosure... [R]easonable detail must be provided in order to enable members of the public to understand and carry out the invention." Genentech, Inc. v. Novo Nordisk Inc., 108 F.3d 1361, 1366, 42 U.S.P.Q.2d 1001, 1005 (Fed. Cir. 1997). The claims, attempt to extrapolate these single findings to any of the above recited conditions In *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993), and MPEP § 2164.08(a). Thus, to determine which, if any, of the

claimed methods would actually provide useful information regarding a particular patient would require of the skilled artisan an unduly burdensome plan of experimentation and research.

Conclusion

This application contains claims 8-11 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX months.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-

0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

January 8, 2006